

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
28 February 2002 (28.02.2002)

PCT

(10) International Publication Number  
**WO 02/15860 A1**

- (51) International Patent Classification<sup>7</sup>: A61K 7/28, 6/00, A01N 43/08, 25/00
- (21) International Application Number: PCT/US01/26058
- (22) International Filing Date: 21 August 2001 (21.08.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
09/645,849 24 August 2000 (24.08.2000) US
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- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**  
— with international search report  
— with amended claims and statement
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



WO 02/15860 A1

(54) Title: TOPICAL ANTIOXIDANT HAVING VITAMIN C AND METHOD OF COMBINATION WITH TOPICAL AGENT BY USER

(57) Abstract: This invention relates to topical reverse aging products containing antioxidants and more specifically to those topical agents and novel methods of creating and maintaining a stable vitamin C composition combined by the user in a pharmaceutically acceptable vehicle such as lotions, creams, solution, sera, and gels, at or near the time of first topical, dermatological use to minimize the degradation of vitamin C and maximize efficacy.

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TOPICAL ANTIOXIDANT HAVING VITAMIN C AND METHOD  
OF COMBINATION WITH TOPICAL AGENT BY USER

## PRIOR RELATED APPLICATIONS

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The present application is a conversion of U.S. Provisional Application Serial No. 60/175,644, filed January 12, 2000, which is incorporated herein by reference in its entirety.

10

## BACKGROUND OF THE INVENTION

## 1. Field of the Invention

This invention relates generally to topical reverse aging products containing antioxidants and more specifically to those topical agents and novel methods of creating and maintaining a stable vitamin C composition combined by the user at or near the time of use for improved product stability.

## 20 2. Description of Related Art

The skin is the largest organ in the body and serves several important functions. The skin retards dehydration and acts as a barrier to the invasion of various pathogens and noxious substances. Skin is composed of the epidermis, or upper layer, and the subjacent dermis. The epidermis is the superficial layer and is composed of several layers. As cells from the deeper layer, the stratum germinativum, move toward the surface, they begin to synthesize the intracellular protein keratin. During subsequent movement, these cells lose their distinct nuclei and form the outermost layer of the epidermis known as the stratum corneum which is comprised of several layers of cornified epidermal cells that are embedded in an intercellular matrix of semi-polar and polar lipids.

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This layer acts as a transport route for various drugs and also acts as a barrier to the transport of other drugs and cosmetics (Elias et al., Journal of Investigative Dermatology 73:339-348, 1979). Skin is subject to abuse by many extrinsic  
5 (environmental) factors. A common extrinsic factor includes exposure to the sun's ultraviolet radiation, the skin damaging effects of which are thought to be caused by the skin's exposure to reactive oxygen species (ROS) including oxygen free radicals. The usual short term effect of UV  
10 exposure is erythema (sunburn) and a long term hazard being premature aging of the skin and risk of cancer. The UV rays penetrate deep into the skin's dermis generating these oxygen-free radicals which can break down collagen, elastin, proteoglycan, potentially even mutate DNA and over time  
15 breakdown connective tissue. This results in wrinkling, yellowing and brown spots of the skin, along with other physical changes such as cracking, telangiectasis (spider vessels), solar keratoses (growths), ecchymoses (subcutaneous hemorrhagic lesions), loss of elasticity, and even skin  
20 cancers. Fortunately, the skin possesses a wide range of interlinked antioxidant defense mechanisms to protect itself from damage by UV induced reactive oxygen species (ROS), such as  $H_2O_2$ , superoxide anion, and singlet oxygen which are thought to be involved in cancer, aging and various  
25 inflammatory disorders. However, the capacity of these defense mechanisms is not unlimited and can be overwhelmed by excessive UV exposure. Thus, to provide photoprotection it may be beneficial to support these endogenous cutaneous oxidative defense systems.

30 Other extrinsic factors such as heating, air conditioning, detergents, and environmental pollution, exert severe stress on the skin, breaking down elastic fibers and accelerating the natural aging process, resulting in

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wrinkles, loss of firmness and elasticity, age spots, discoloration, dryness, and other cosmetically undesirable effects. Among the most damaging pollutants are hydrogen chloride, formaldehyde, chloroform, sulfur dioxide, carbon  
5 monoxide, tobacco smoke, car exhaust fumes, and nitrogen dioxide. Other environmental effects that can damage skin are oxygen deprivation (anoxia) and formation of free radicals.

Skin is exposed to a variety of intrinsic (chronoaging) factors as well which result in the thinning and general  
10 degradation of skin. As the skin naturally ages, there is a reduction in the cells and blood vessels that supply the skin. There is also a flattening of the dermal-epidermal junction which results in weaker mechanical resistance of this junction.

15 With increasing age, the skin gradually loses ceramides and water and becomes drier, less flexible and supple, more wrinkled, and scaly in appearance.

The supporting dermis of the skin is known to thin with age and sun exposure. Since the dermal layer provides the  
20 support and blood supply for the epidermis, it is of critical importance in maintaining the elasticity and appearance of the skin. Disruption of the supporting dermis layer leads directly to sagging and consequent furrowing of the epidermis, i.e., the formation of wrinkles.

25 Deep wrinkles are due to continual stretching and contraction of both the dermis and epidermis, and such deep furrows can only be eliminated by plastic surgery or by collagen injections directly beneath the depressed areas. However, fine wrinkles which occur with age (and repeated  
30 prolonged exposure to the sun) on skin areas which are less stretched during use are the direct result of deterioration of the supporting dermal layer. Thus during the aging process and in instances where that process has been

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accelerated by incident radiation, there is disruption of the collagen bundles which collectively provide support to the epidermis. It is the stimulation of collagen formation which is believed to be one of the benefits imported by vitamin C.

5       One of the major objectives of the cosmetic industry is to reduce and retard the drying and wrinkling of the skin that occurs with aging or as the result of exposure to wind, sun, cold and chemicals. Many people view skin wrinkles as a reminder of the disappearance of youth, hence the elimination  
10 of wrinkles has become a booming business in youth-conscious societies. As the mean age of the population rises, more people are seeking products that will retard and reduce the effects of aging on the skin and will essentially rejuvenate the skin.

15       L-ascorbic acid, commonly known as vitamin C, an antioxidant, is known to prevent ultraviolet (UV) damage to the skin by absorbing UV radiation. Upon exposure to UV radiation, levels of vitamin C are depleted as are most cutaneous antioxidants which are known to counteract the skin  
20 damaging effects of the above mentioned superoxide and hydroxyl radicals. These radicals destroy lipid membranes, break down DNA and inactivate beneficial enzymes which promote healthy skin conditions. Free radicals from ultraviolet light (UV) are known to increase with air  
25 pollution in areas of concentrated populations, thereby magnifying the problem. The free radicals hydrolyze elastin fibers in the skin and desynthesize collagen in the lower dermal layers of the skin, thereby causing skin wrinkles and other damaging skin conditions. In contrast, ascorbic acid is  
30 believed to be effective in counteracting the effects of free radicals upon the skin thereby acting as a photoprotectant and at the same time stimulating collagen, the major fibrillar component of dermal connective tissue, comprising

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approximately 70-80% of the dry weight of the dermis. See Murad, S., Grove, D., Lindberg, K. A., Reynolds, G., Sivarajah, A., Pinnell, S. R., "Regulation of Collagen Synthesis by Ascorbic Acid", Proc. Natl. Acad. Sci. 78 (5): 2879-2882 (1981). More recent studies indicate that ascorbic acid encourages the synthesis of procollagen by stimulating procollagen mRNA. See Freiburger, H., Grove, D., Sivarajah, A., Pinnell, S. R., "Procollagen I Synthesis in Human Skin Fibroblasts: Effect of Culture Conditions on Biosynthesis", J Invest. Derm. 75: 425-430 (1980); Tajima, S., Pinnell, S. R., "Regulation of Collagen Synthesis B., Ascorbic Acid. Ascorbic Acid Increases Type I Procollagen mRNA", Biochem Biophys Res. Comm. 106 (2): 632-637 (1982). Ascorbic acid acts as an oxidation-reduction agent and participates in the formation of collagen essential for body growth, tissue repair and wound healing. It has very low toxicity to humans.

Other studies indicate that ascorbic acid helps increase membrane lipid peroxidation and antioxidation. Girotti, A. W., Thomas, J. P., Jordan, J. E., "Prooxidant and Antioxidant Effects of Ascorbate on Photosensitized Peroxidation of Lipids in Erythrocyte Membranes", photochem. Photobio 41 (3): 267-276 (1985).

Ascorbic acid also may assist in inhibiting the production of melanin responsible for skin discolorations. Tomita, Y., Hariu, A., Mizumo, C., and Seyi, M., "Inactivation of Tyrosinase by Dopa", J. Invest. Derm. 75 (5): 379-382 (1980) Finally, ascorbic acid may prevent the accumulation of histamine in body tissues responsible for many allergenic reactions. Bates, C. J., "The Function and Metabolism of Vitamin C in Man" Vit C Ascorbic Acid, Counsell, J. N., Horning, D. H., eds., Applied Sci. Publishers.

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By providing pharmacological levels of L-ascorbic acid targeted topically to the skin, environmental oxidative insults e.g. sunlight, smoking, and pollution, are interfered with. The benefits of L-ascorbic acid (vitamin C) include  
5 neutralizing reactive oxygen species, regenerating vitamin E, stimulating collagen growth, preventing immunosuppression and as an anti-inflammatory agent. U.S. Patent No. 4,938,969 to Schinitzky discloses a method for treating skin damage and photoaged skin with the attendant diminution of fine wrinkles  
10 when a composition containing ascorbic acid is topically applied.

Topical application of vitamin C has been reported to alleviate UVA and UVB radiation induced skin damage. Darr, et al., Br. J. Derm., 1992. The mechanism of protection  
15 seems to be two fold. First, ascorbic acid directly quenches or reacts with singlet oxygen, hydroxyl radicals and superoxide anions. Halliwell and Gutteridge, Arch. Of Biochem. & Biophys., 1990. Secondly, it supports the action of alpha tocopherol (vitamin E) by regenerating tocopheroxyl  
20 radicals. Since vitamin C is present in the skin in much higher amounts than alpha tocopherol, it acts as a large reservoir of antioxidant potential that is delivered by the more specific alpha tocopherol. Topical vitamin C prevents UV immunosuppression as published by Nakamura, T. et. al. in J.  
25 Invest. Dermatol., 1997. This phenomenon, in which the activity of the immune system is stifled following exposure to sunlight, occurs in approximately one third of humans and in over 90 percent of individuals diagnosed with melanoma and non-melanoma skin cancers. See Granstein, R., Arch.  
30 Dermatol., 1995 and Streilein, W. et.al. in Photoprotection, 1995. When skin is immunosuppressed, it is paralyzed in its ability to respond to sensitizers, such as poison ivy. Studies show that topical L-ascorbic acid prevents the loss

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of contact hypersensitivity in animals exposed to UV radiation and also prevents UVB induced tolerance. Skin inflammation is mediated by reactive oxygen species. Vitamin C is rapidly depleted when skin is inflamed and needs to be replaced.

Because of these many beneficial effects, it is a desirable objective to percutaneously deliver effective concentrations of ascorbic acid directly to the skin's underlying tissue matrix (i.e. the dermal layer) via a topically applied, cosmetically elegant carrier or base.

Prior art has discussed treatment of photo-aged skin, wrinkles and other sequelae associated with aging, with ascorbic acid and related derivatives and such treatment commonly involved the topical application of ascorbic acid to affected areas of the skin in lotions, creams and other delivery vehicles, such as discussed in U.S. Patent No. 5,843,411 to Hernandez, et.al.

However, due to its alpha-keto lactone structure, ascorbic acid is very sensitive to the influence of environmental parameters such as light, oxygen, and water. An unavoidable degradation of ascorbic acid in solution occurs over time due to its pH and the presence of trace metals. This problem has been addressed in a variety of ways in the art. In order to reduce or delay the degradation of ascorbic acid in solution, U.S. Pat. No. 5,140,043 to Darr recommends stabilization by introducing ascorbic acid into aqueous-alcoholic solutions, formed of at least 80% water and having a pH below 3.5.

Although ascorbic acid is readily soluble in water, it oxidizes rapidly in aqueous solutions, and thus cannot be stabilized in sufficient concentration in such media to achieve skin appearance enhancement effects. The instability of ascorbic acid was shown in, Darr '043 with drops in



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potency of L-ascorbic acid of less than 10 percent over seven weeks at room temperature for L-ascorbic concentrations of three (3), five (5) and ten (10) percent respectively, and a drop in potency of approximately 30 percent over seven weeks, of L-ascorbic acid in a concentration of one (1) percent. Darr '043 also shows all four samples of L-ascorbic acid having lost potency of at least ten (10) percent over eight (8) weeks at room temperature, when stored in the dark. Solubility of ascorbic acid in non-aqueous media on the other hand is quite limited, thereby preventing an anhydrous base from achieving the desired level of stability and efficacy. For these reasons, unstabilized ascorbic acid heretofore has been used in cosmetic formulas only in trace amounts of less than about 0.1% by weight to serve as an antioxidant, and prior attempts to develop and market an acceptable cosmetic formulation containing efficacious concentrations of stabilized ascorbic acid have failed.

Ascorbic acid, L-ascorbic acid, and/or Vitamin C are the equivalent trivial chemical names given to a white odorless crystalline solid having the formula  $C_{sub.6}H_{sub.8}O_{sub.6}$ . Ascorbic acid is relatively soluble in aqueous media, and relatively insoluble in organic solvents such as alcohol, glycol, fats and oils.

The human body does not manufacture ascorbic acid and must obtain it from outside sources in order to survive. Ascorbic acid levels in humans tend to decrease with age. Collagen levels also decrease accompanied by changes in morphology. The fibers become more intermittent and thinner resulting inevitably in surface skin effects such as dryness, flaking, wrinkling and loss of luster and elasticity. See Eyre, D. R. (1980), "Collagen Molecular Diversity in the Body's Protein Scaffold", Science, Vol. 207: 1315-1322; Wright, E. T., Shellow, W. V. (1973), "The Histopathology of

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Wrinkles", J. Soc. Cosmetic Chem. 24: 81-85; and Sinex, F. M. (1968)", "Role of Collagen in Aging", In Treatise on Collagen, Vol 2, Biology of Collagen edited by B. S. Gould, Part B. Academic Press. Exposure to ultraviolet light also  
5 has a tendency to interfere with collagen synthesis causing skin to exhibit the effects of premature aging. See Semma, M., Sasaki M. (1978) "Aging of Skin - Changes of the Dermal Connective Tissue", Cosmetics and Toiletries, Vol. 93:29-36.

We believe in accordance with the present invention that  
10 replenishment of the dermal tissues with ascorbic acid mixed by the consumer at or near the time of first use over a limited period of time and delivered percutaneously through the stratum corneum can impart beneficial appearance effects to skin, i.e. improved tone and luster, a decrease in fine  
15 lines and wrinkles, improved elasticity, and minimize vitamin C instability, i.e loss of potency and color and so on. As a suitable base or carrier for the ascorbic acid, a composition comprising stabilized aloe vera gel is provided having desirable skin soothing and anti-inflammatory qualities. Any  
20 viable over the counter consumer product requires in excess of twelve weeks from manufacture through distribution points to final retail sale, and must still afford the consumer a reasonable time to consume the contents of the product. Therefore, serious questions arise as to the stability and  
25 the usefulness of a manufactured product containing ascorbic acid during the time the consumer is able to use the product. Thus it is important to minimize the time exposure of the ascorbic acid to most pharmaceutical vehicles so as to maximize the potency and efficacy of the desired effects of  
30 the ascorbic acid topically on the skin.

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## SUMMARY OF THE INVENTION

This invention relates to dermatological compositions and methods for topical application to human skin, which is believed to provide medical prevention, physical protection and cosmetic restoration properties, resulting from the effects of the aging process, containing Vitamin C which is separately packaged and physically combined by the consumer at or near the time of use, in a pharmaceutically and therapeutically acceptable carrier or vehicle, containing suitable solvents, moisturizers, humectants, chelators, exfoliants, emulsifiers, thickeners, surface active agents, antioxidants, soothing agents, fragrances, preservatives, and the like.

Another embodiment of the present invention comprises a method of treating human skin comprising the step of topically applying to the human skin, a composition comprising Vitamin C combined with a pharmaceutically acceptable carrier by the consumer at or near the time of first use which final stable composition is thereafter applied to the skin over a period of about two weeks, until initial mixed quantity is totally consumed and then the process is repeated.

The present invention relates to compositions and methods for photoprotection and reduction of wrinkles in human skin comprising a safe and effective amount of ascorbic acid with one or more active agents selected from the group consisting of a safe and effective amount of an anti-inflammatory agent, hydroxy acid, anti-oxidant, chelator, retinoid, moisturizer, and a skin protectant, derivatives thereof and mixtures thereof in a diluent carrier.

In one embodiment, the present invention provides an easy to use therapeutic and cosmetic process for treating and reversing the adverse effects on the skin caused by the aging

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process by combining and topically applying the compositions disclosed herein. Use of the disclosed process and composition is believed to increase the moisture content of the skin, reduce and retard wrinkling, provide a rejuvenated appearance to the skin and bind skin damaging free radicals while maximizing the stability and activity of the separately packaged vitamin C which is combined by the consumer with small portions of the topical carrier at or near the time of initial use by consumer.

10       The present invention provides methods and compositions for topically treating damaged skin tissue resulting primarily from aging, but also may treat and prevent further damage which has been caused chemical drying, wind, sun, fire, cold, and chemicals.

15       It is an object of the present invention to provide methods and compositions for regulating wrinkles in human skin which comprise a safe and effective amount of anti-wrinkle, antioxidant, and photoprotective agent which is stable during the period of use by the consumer.

20       Accordingly, it is an object of this invention to provide compositions and methods which will overcome the shortcomings of prior methods and preparations which were ineffective and otherwise of little or no utility due to short shelf life and vitamin C instability.

25       It is another object of the present invention to provide stable compositions and methods which will reduce, prevent repair and reverse the adverse effects of the aging process on skin.

30       Another object of this invention is to provide shelf stable compositions and the methods of use which will contain safe and effective protectant, moisturizing and demulcent ingredients combined with vitamin C by user to soften, protect, repair damaged skin, to stimulate growth of healthy

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tissue, and to even reverse dermal damage caused by the aging process, extrinsic, and intrinsic factors.

Yet another object of this invention is to provide compositions and the method of use which will contain  
5 ingredients to penetrate the skin and to compensate for the diminished anti-oxidants. Still another object of the present invention is to provide shelf stable ascorbic acid compositions and methods of use for skin treatment in a  
10 pharmaceutically acceptable vehicle combined at or near the time of use by the consumer which could also include cosmetically effective moisturizers and humectants to promote softness, retain moisture, act as emollients and to halt and even reverse dermal damage caused by the aging process.

A further object of the present invention is to provide  
15 compositions of the types described in which the main active ingredient, Vitamin C in a separately packaged form is added to the pharmaceutically acceptable carrier at or near the time of first use by the consumer and remains shelf stable for a period consistent with the amount time necessary to  
20 consume the product so combined so as to permit proper commercial exploitation and product efficacy over the expected period of use.

It is another object of the invention to provide a term  
of use stable pharmaceutically acceptable composition and  
25 method for reducing the damaging effects of aging on human skin.

It is another object of the invention to provide a method for topically applying Vitamin C to the human skin in a soluble, and stable form, readily absorbable and combined  
30 by the consumer at or near time of first use to reduce the signs and effects of the aging process while reducing the likelihood of vitamin C instability.

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It is therefore an object of the present invention to provide a stable composition and pharmaceutical delivery system and method for skin application of ascorbic acid, ascorbic acid derivatives and/or extracts containing ascorbic acid as effective treatments for age related wrinkling and skin disorders.

It is yet a further object to provide a stable topical delivery method for ascorbic acid, derivatives of ascorbic acid and/or extracts containing ascorbic acid, added by consumer at or near time of first use so as to decrease the vitamin C instability in the product at the time it is utilized by the consumer.

It is yet a further object to provide ascorbic acid, ascorbic acid derivatives and/or extracts containing ascorbic acid, in a composition wherein the ascorbic acid is added by the consumer at or near the time of use and which remains effective over the period of time anticipated for use by the consumer.

It is yet another object to improve over the disadvantages associated with the topical application of vitamin C to the human skin as previously encountered in the prior art. Other objectives and advantages will appear as the specification proceeds.

In keeping with these objects and others which may become apparent, according to the present invention, a new stable, composition and method is provided for the pharmaceutical delivery of ascorbic acid, ascorbic acid derivatives and/or extracts containing ascorbic acid, to prevent and treat sun-damaged and photo-aged skin, reduce wrinkling and as a UV protectant and cosmetic for damaged and undamaged human skin.

As used herein are the following items:

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"Moisturize" or derivatives thereof, relates to the conservation or enhancement of the water with reference to the skin.

"Topical application" is used to mean direct local  
5 administration of the composition to the skin.

"Pharmacologically active agent" relates to any chemical material or compound suitable for topical administration which includes any desired local effect on human tissue contacted therewith.

10 "Safe and effective amount" means an amount of compound or composition sufficient to significantly induce a positive modification in the condition to be treated, but low enough to avoid serious side effects (at a reasonable benefit/risk ratio), within the scope of sound medical judgment. The safe  
15 and effective amount of the compound or composition will vary with the particular condition being treated, the age and physical condition of the patient being treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, the specific compound or composition  
20 employed, the particular pharmaceutically-acceptable carrier utilized, and like factors within the expertise of a physician.

"Regulating wrinkles" as used herein means preventing, retarding, arresting, or reversing the process of wrinkle  
25 formation or effects of aging on skin.

"Pharmaceutically acceptable carrier" is used herein to mean any liquid, gel, salve, solvent, liquid, diluent, fluid, ointment base, liposome, serum, micelle, and the like, which is suitable for use in contact with human tissue  
30 without causing undue toxicity, incompatibility, instability, irritation, allergic or adverse physiological responses, and which does not interact with other components of the

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composition in a deleterious manner and having a reasonable risk/benefit ratio.

As used herein the terms "solution", "preparation", "composition", "formulation", and "formula" are to be construed interchangeably.

The terms "cosmetic" or "cosmetic preparation" or "cosmetic composition" as used herein, means (i) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human or animal body or any part thereof for cleaning, beautifying, promoting attractiveness, or altering the appearance, and (ii) articles intended for use as a component of any such articles, e.g. sun screening compositions, medicinal or first aid creams, and so on.

A method of preventing and/or treating photo-aged skin, wrinkles and aging related skin disorders is provided by topical application of a lotion, cream, gel, solution or serum formulation in which the consumer combines effective amounts of ascorbic acid, ascorbic acid derivatives and/or extracts containing ascorbic acid at or near the time of first use dissolved within the pharmaceutically acceptable carrier for topical skin application.

Ascorbic acid, or its derivatives, such as ascorbic palmitate, sodium ascorbate, potassium ascorbate, ammonium ascorbate, triethanolamine ascorbate, ascorbyl phosphate or magnesium ascorbyl phosphate and related compounds, in combination and separately packaged is combined by the consumer at or near the time of use with a pharmaceutically acceptable vehicle, and applied to the skin in a concentration of from 0.1 percent by weight to 99.9 percent by weight, preferably 10-15 percent by weight, generally by frequent periodic application, such as once or twice daily and for periods as long as the consumer desires up to and



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including throughout life. The preparation is packaged in quantities designed to be totally consumed by user within about two weeks after which time a fresh batch is combined for further use on a repeated basis thereby allowing the  
5 vitamin C contained within the final combination composition to remain in a stable and active form throughout the anticipated usual period of use by the consumer.

Instead of being combined with the vehicle at the time of manufacture, the ascorbic acid, ascorbic acid derivatives  
10 and/or extracts containing ascorbic acid are provided separately packaged, to be added by the consumer. The pharmaceutically acceptable carrier is not water free, but is substantially anhydrous, that is the water content does not  
15 generally exceed five (5) percent by weight of the total composition. The minimal water content in the vehicle and combination by the consumer of the separately packaged ascorbic acid, ascorbic acid derivatives and/or extracts containing ascorbic acid at or near the time of use reduces the potential that the ascorbic acid, or its derivatives  
20 and/or extracts containing ascorbic acid, will degrade, become instable, lose of potency or change color.

The pharmaceutically acceptable carrier comprises any substantially anhydrous diluent, vehicle, or composition known with in the art, and as referenced above and includes  
25 for example, stabilized aloe vera gel, in a range of from 0.1 percent by weight to 99.9 percent by weight, preferably about 70 to 80 percent by weight. Stabilized aloe vera gel can be obtained from Active Organics in Louisville, Texas or other suppliers readily known within the industry or as set forth  
30 in U.S. Patent No. 3,892,853 to Cobble and U.S. Patent No. 4,178,372 to Coats.

Other pharmaceutically acceptable carriers and pharmacologically active agents may be used or included, such

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as other emollients, emulsifiers, surfactants, binders, anti-oxidants, exfoliating agents, moisturizers, anti-microbials, exfoliating agents, chelating agents, preservatives, demulcents, humectants, viscosity control aids, PH buffers, and carrier solvents.

The resultant mixture delivers the ascorbic acid or its derivatives to the skin in an effective and stable manner.

#### DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is directed to compositions and methods for topical skin application to reduce wrinkling resulting from intrinsically and extrinsically induced aging. The compositions preferably comprise from about 1 to about 20%, and more preferably about 5 to about 15% ascorbic acid. At or near the time of use by the consumer, the separately packaged vitamin C component is preferably added to and blended (usually by shaking the container gently) into a tissue compatible carrier, such as hydrophilic lotion-, cream-, serum-, or gel-based vehicle. Such pharmaceutically acceptable carriers are well known in the art and commercially available for formulation of active ingredients into a suitable form for topical application.

In accordance with the present invention, a stable composition in a pharmaceutical acceptable carrier for topical delivery of ascorbic acid or its derivatives, extracts, and esters to reduce, repair and prevent age and environmentally-related damage to skin, wrinkles, and for skin disorders associated with the aging process is provided which is shelf stable during the expected period for total consumption by the user of the blended product.

A method of treating photo-aged skin, sunburn, wrinkles and related skin disorders is also provided by topical application of a lotion, cream, gel, solution or serum

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applied formulation, preferably a substantially anhydrous composition, containing effective amounts of a compound selected from the group consisting of ascorbic acid, ascorbic acid derivatives and/or extracts containing ascorbic acid,  
5 for topical skin application.

Ascorbic acid, or its derivatives, such as ascorbyl palmitate, sodium ascorbate, potassium ascorbate, ammonium ascorbate, triethanolamine ascorbate, ascorbyl phosphate or magnesium ascorbyl phosphate, ascorbic acid polypeptides,  
10 ascorbyl glucosamine, ascorbic acid polymers, esters of ascorbic acid, amides of ascorbic acid, L-ascorbic acid, known as vitamin C, or other derivatives, or related compounds, is separately packaged, and combined by the consumer at or near the time of first use in a  
15 pharmaceutically acceptable vehicle, in a concentration of from 0.1 to 99.9 percent by weight, preferably 10-15 percent by weight, then topically applied to the skin periodically such as once or twice daily.

The method comprises steps of mixing together by the  
20 consumer at or near the time of use, separately packaged ascorbic acid, its derivatives, esters or extracts containing ascorbic acid with a substantially anhydrous vehicle base and the topical application of the resulting composition, preferably once or twice daily over approximately a two-week  
25 period, then new batches can be mixed one by one, as needed and at or near the time of first use and again repeatedly applied to the skin until totally consumed over a period including throughout the life of the user. This method minimizes and protects against the instability, degradation  
30 and loss of potency inherent with ascorbic acid when combined with a topical pharmaceutical vehicle. The limited period of anticipated use of each batch as blended by consumer thereby maximizes vitamin C efficacy since only approximately the

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amount of carrier to be used over a two week period is provided for each batch prepared, ie. approximately 30 cc.

In general, the composition suitable for use in accordance with the invention containing ascorbic acid, its derivatives, esters, or extracts may be added to any substantially anhydrous dermatological acceptable vehicle such as a gel, lotion, cream, serum or solution applied formulation which will allow the ascorbic acid to disburse or dissolve, said vehicle may or may not be emulsified and may contain ingredients to improve, modify, or stabilize the formulation physically or cosmetically. Other suitable formulations will be apparent to those skilled in the art.

Emulsifiers such as triethanolamine and isocetheth-20 and chelating agents such as tetrasodium EDTA, may also be used to further stabilize other substantially anhydrous bases. Fat soluble vitamins/anti-oxidants such as Vitamins A and E and their esters or derivatives, may also be included in the carrier to which the ascorbic acid is added by the consumer. Buffers generally utilized within the art may also be added to adjust the pH of the final composition. Other components may include preservatives, humectants, viscosity control aids, fragrance, and carrier solvents.

The method of treatment with the compositions of the invention is believed to reduce wrinkling and improve the overall condition of aging skin to which it is applied, preferably by frequent periodic application over an extended period of time without undue skin irritation.

Table 1 shows the stability of samples of the composition containing 5% and 10% ascorbic acid. The compositions were tested for stability of color, separation, and fragrance at an elevated temperature of 45°C and tested for color changes, an indicator of vitamin C degradation, at room temperature for the 10% ascorbic acid composition.

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Testing at 45°C, for one month is believed to be substantially equivalent to exposure at room temperature for approximately one year.

TABLE 1

5

**COMPOSITION 1**

A topical dermatological fluid containing 5% of L-ascorbic acid.

10 a) Condition: maintained at 45 degrees Centigrade in a 1 ounce clear, colorless, glass container.

b) Test: stability based on color and appearance

|    |               |                |
|----|---------------|----------------|
|    | <u>0 days</u> | <u>33 days</u> |
|    | clear         | cloudy         |
| 15 | colorless     | dark amber     |
|    | no separation | no separation  |

**COMPOSITION 2**

20 A topical dermatological fluid containing 10% of L-ascorbic acid.

a) Condition: maintained at 45 degrees Centigrade in a 1 ounce clear, colorless, glass container.

b) Test: stability based on color and appearance

|    |                 |                      |
|----|-----------------|----------------------|
| 25 | <u>0 days</u>   | <u>7 days</u>        |
|    | clear           | clear                |
|    | slightly yellow | darker yellow/orange |
|    | no separation   | no separation        |

**COMPOSITION 3**

A topical dermatological fluid containing 10% of L-ascorbic acid.

a) Condition: maintained at room temperature in a 1 ounce clear, colorless, glass container.

35 b) Test: stability based on color and appearance

|    |                 |                 |
|----|-----------------|-----------------|
|    | <u>0 months</u> | <u>7 days</u>   |
|    | clear           | clear           |
|    | slightly yellow | slightly yellow |
| 40 | no separation   | no separation   |

A comparison was also made of the changes in color that occurred with time after mixing four other compositions. The following four solutions were prepared and any color changes

45

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were quantified against a defined standard. The four solutions were prepared as follows:

- 1) Sample A with no vitamin C mixed;
- 2) Sample B immediately after mixing 10% by weight vitamin C;
- 3) Sample C with 10% by weight Vitamin C mixed, aged 2 weeks stored at room temperature without exposure to light or opening of container.
- 4) Sample D with 10% by weight Vitamin C mixed, aged 4 weeks stored at room temperature without exposure to light or opening of container.

The color changes were then reviewed three times by three blinded observers against a color graded standardized color scheme to determine varying percentages of yellow. The three observations of each observer were then averaged.

All values contained within the table below are given as percentage yellow as determined against a graded color scale, defined by Adobe Photoshop. All observations were performed in the same room lighted by a halogen bulb. All the observers had adequate time to make their observations and there was at least a 15 minute interval between each set of observations taken by each observer in order to avoid eye fatigue. Data was recorded by a person other than the one who made the observation after all four solutions were graded. These solutions were compared against a color video monitor (Sony Triniton Ultrascan p.991) with the graded color scale mentioned above.

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Table 2

|                   | Observation 1 | Observation 2 | Observation 3 | AVG  |
|-------------------|---------------|---------------|---------------|------|
| <b>Observer 1</b> |               |               |               |      |
| Sample A          | 0             | 0             | 0             | 0    |
| Sample B          | 0             | 0             | 0             | 0    |
| Sample C          | 17            | 20            | 17            | 18   |
| Sample D          | 23            | 27            | 26            | 25.3 |
| <b>Observer 2</b> |               |               |               |      |
| Solute A          | 0             | 0             | 0             | 0    |
| Solute B          | 0             | 0             | 0             | 0    |
| Solute C          | 18            | 19            | 19            | 18.7 |
| Solute D          | 24            | 25            | 24            | 24.3 |
| <b>Observer 3</b> |               |               |               |      |
| Solute A          | 0             | 0             | 0             | 0    |
| Solute B          | 0             | 0             | 0             | 0    |
| Solute C          | 18            | 18            | 17            | 17.7 |
| Solute D          | 25            | 25            | 26            | 25.3 |

5

|          | Average | Range | Standard Deviation |
|----------|---------|-------|--------------------|
| Solute A | 0       | 0-0   | 0                  |
| Solute B | 0       | 0-0   | 0                  |
| Solute C | 18.1    | 17-20 | 1.05               |
| Solute D | 25.0    | 23-26 | 1.22               |

Percentage average color change from week 2 to week 4  
(25/18.1= 1.38) was 38%.

10

The Vitamin C solution showed a time dependent yellowing that was marked, and easily observable by blinded testers. The color changes were quantified under controlled conditions, and the results tabulated. The solution that had no vitamin C added to it had no color change, despite being aged. Solution that had Vitamin C added to it and was immediately observed also had no color change. Therefore the conclusion is made that Vitamin C in the carrier undergoes a color change that correlates with time dependent oxidation (degradation) quantifiable by independent observers. These results are within a reasonable standard deviation. These results are also consistent with the fact

20

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that vitamin C in solution undergoes a time dependant degradation. Incidentally, a sample of the carrier combined with vitamin C that was more than 4 months old was markedly yellow/brown. This sample was not compared against the  
 5 graded color scale because the exact date the vitamin C was combined with the carrier was not known.

The compositions of this invention are prepared in any desired manner and in any suitable order or sequence of addition of the various components and those skilled in the  
 10 art will be readily cognizant of those available mixing procedures which are operative for ease and speed of production of such compositions.

Table 3 illustrates a composition of the present invention in the preferred cosmetic and dermatological form  
 15 and typical ranges of acceptable percentages of each ingredient. The composition may also be provided in the form of a cream, emulsion, lotion, serum, solution, or gel. A thin layer of such composition should be applied and rubbed into the skin regularly, preferably once or twice daily, up  
 20 to one ounce per application depending on the size of the area to be covered.

TABLE 3

| 25 | Ingredient               | Preferred<br>% by weight | Phase | Ranges               |     |
|----|--------------------------|--------------------------|-------|----------------------|-----|
|    |                          |                          |       | Typical<br>of Ingred |     |
|    | stabilized aloe vera gel |                          | 72.00 | A                    | 50- |
|    | 99.9                     |                          |       |                      |     |
| 30 | methylparaben            |                          | 0.20  | A                    |     |
|    | 0.0-5.0                  |                          |       |                      |     |
|    | tetrasodium EDTA         |                          | 0.10  | A                    |     |
|    | 0.0-5.0                  |                          |       |                      |     |
| 35 | isocetheth-20            |                          | 2.50  | B                    |     |
|    | 0.0-5.0                  |                          |       |                      |     |
|    | fragrance                |                          | 0.05  | B                    |     |
|    | 0.0-5.0                  |                          |       |                      |     |



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|    |                               |       |   |
|----|-------------------------------|-------|---|
|    | tocopherol acetate(vitamin E) | 0.50  | B |
|    | 0.0-20                        |       |   |
|    | retinyl palmitate (vitamin A) | 0.10  | B |
|    | 0.0-2.0                       |       |   |
| 5  | deionized water               | 1.00  | C |
|    | 0.0-1.5                       |       |   |
|    | diazolidinyl urea             | 0.30  | C |
|    | 0.0-2.0                       |       |   |
| 10 | hyaluronic acid               | 0.50  | D |
|    | 0.0-2.0                       |       |   |
|    | chamomile extract             | 0.10  | D |
|    | 0.0-5.0                       |       |   |
| 15 | calendula extract             | 0.10  | D |
|    | 0.0-1.0                       |       |   |
|    | green tea extract             | 0.10  | D |
|    | 0.0-5.0                       |       |   |
|    | arnica extract                | 0.10  | D |
| 20 | 0.0-1.0                       |       |   |
|    | deionized water               | 0.20  | E |
|    | 0.0-1.5                       |       |   |
|    | sodium metabisulfite          | 0.25  | E |
| 25 | 0.0-2.0                       |       |   |
|    | triethanolamine               | 5.00  | F |
|    | 0.0-10                        |       |   |
|    | glycolic acid                 | 5.00  | F |
| 30 | 0.0-70                        |       |   |
|    | vitamin C                     | 10.00 | G |
|    | 0.1-50                        |       |   |
|    | MSM                           | 0.10  | G |
| 35 | 0.0-5.0                       |       |   |

# I. NATURE AND PROPORTION OF INGREDIENTS OF THE SKIN COMPOSITION

Each of the cosmetic components disclosed contributes  
40 to  
the improved properties and functioning of the compositions  
and methods of the present invention. Only items 1 and 3  
below are required the others are optional.

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Preferred compositions are now disclosed. However, other compositions containing the required ingredients set forth herein are possible and are within the scope of the present invention.

5 1. Ascorbic Acid Component

The ascorbic acid component can be selected from the group consisting of ascorbyl myristate, ascorbyl palmitate, ascorbyl stearate, ascorbic acid L-ascorbic acid, ammonium ascorbate, potassium ascorbate, sodium ascorbate, ascorbyl  
10 phosphate, magnesium ascorbyl phosphate, triethanolamine ascorbate or other derivatives commonly known in the art and mixtures thereof. Preferably, the composition contains between 5-15% of ascorbic acid. Methylsulfonylmethane (MSM), a topical anti-inflammatory agent, may be optionally added to  
15 the ascorbic acid component and has been used topically as anti-inflammatory and to accelerate healing.

2. Carrier/Solvent Component

A safe and effective amount of a pharmaceutically  
20 acceptable carrier is from about 50% to about 99.9%, preferably from about 50% to about 75%, more preferably from about 75% to about 80%, of the composition. The preferred carrier is stabilized aloe vera gel which allows greater uniformity and ease of distribution of the ascorbic acid  
25 within the preparation

Aloe vera, a tropical or subtropical plant whose leaves contain a viscous but essentially clear gel which has been safely used for a variety of medicinally purposes, e.g. as a tonic, cleanser, anesthetic, antiseptic, antipyretic,  
30 antipruritic, moisturizer, vasodilator, anti-inflammatory and promoter of cell proliferation, however, therapeutic qualities of the clear gel of the aloe vera depends on the freshness of the gel. The gel exerts a soothing and calming

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effect on skin. In addition to loss of therapeutic efficacy on aging, decomposition products occur after a short time that may make the natural gel even less useful than it might be. Commercially available gel extracts are most difficult to compound into cream bases for topical application because the decomposition products tend to bring about a separation of the cream emulsion. Attempts to take advantage of the qualities of the gel in cosmetic preparations have been frustrated since such formulations become discolored, rancid or malodorous after about a month, adversely affecting their cosmetic utility. To avoid these problems a stabilized form of aloe vera gel is preferred and commercially available from Active Organics located in Louisville, Texas.

The topical use of anti-inflammatory agents to alleviate erythema is known. Compositions containing steroidal anti-inflammatories, non-steroidal anti-inflammatories, as well as "natural" anti-inflammatories, such as extract of the plant Aloe Vera, have been disclosed in prior art for such use. Short-term application of anti-inflammatory agents prior to UV exposure to prevent erythema, as well as application after UV exposure to lessen UV-induced damage to skin, has been taught. See, e.g. U.S. Patent No. 4,185,100 to Rovee, U.S. Patent No. 4,847,071 to Bissett, and U.S. Patent No. 4,338,293 to Holick.

25

### 3. Humectant-Moisturizer

Hyaluronic acid is a major component of the extracellular matrix and participates in a number of important biological processes such as cell mobility, cell differentiation, wound healing and cancer metastasis. It acts as a humectant and moisturizer. The acceptable range of amounts is between 0.01 and 2.00%, preferably 0.5%

30

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weight/volume. Other humectants and moisturizers commonly known in the cosmetic art may be used.

#### 4. Anti-Free Radical Component

5           The final cosmetic composition of the present invention also includes antioxidants to protect the skin against free radicals, typically comprising a long-chain fatty acid ester of retinol, and a short-chain carboxylic acid ester of tocopherol.

10           Preferably, the long-chain fatty acid ester of retinol is selected from the group consisting of retinyl palmitate, retinyl myristate, retinyl acetate retinyl stearate, or other commonly known derivative of vitamin A, most preferably, retinyl palmitate all of which are readily commercially

15 available. The therapeutic action of vitamin A in its acid (retinoic acid), aldehyde (retinal) or alcohol form (retinol) is well known in dermatology. U.S. Patent No. 4,603,146 to Kligman discloses methods for repairing UV-induced damaged skin through by the topical application of retinoic acid. The

20 fatty acid esters of vitamin A have the advantage of being well tolerated by the skin and the organism. The concentrations of the ester of vitamin A can be advantageously used at a concentration ranging from 1,000 to 10,000 international units (IU: expressed as vitamin A) per

25 gram of the composition. In a preferred wrinkle regulating composition of the present invention, the retinoid, retinyl palmitate, is preferably included as an active agent along with the active vitamin C component. The inclusion of a retinoid (vitamin A derivative) increases the wrinkle

30 regulating benefits of the composition. A safe and effective amount of a retinoid may be added to the compositions of the present invention, preferably from about 0.001% to about 2%, more preferably from about 0.01% to about 1% of the

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composition. As used herein, "retinoid" includes all natural and/or synthetic analogs of Vitamin A or retinol-like compounds which possess the biological activity of Vitamin A in the skin as well as the geometric isomers and stereoisomers of these compounds.

#### 5. The Tocopherol Component

The tocopherol component is selected from the group of short chain carboxylic acid ester of tocopherol consisting of tocopherol acetate, tocopherol butyrate, tocopherol succinate, tocopherol oleate, tocopherol propionate. Most preferably, the short-chain fatty acid ester of tocopherol is tocopherol acetate and comprises up to 5.0% of the composition.

Tocopherol (Vitamin E) has been disclosed for use as a photoprotector in topical compositions. See, e.g., U.S. Patent No. 4,144,325 to Voyt. Tocopherol works to protect the skin from deleterious effects of UV-irradiation. However, cosmetic industry experience suggests that tocopherol may have stability problems, specifically oxidation problems. One frequently used approach to address these problems involves the formulation of compositions including esters of tocopherol, these esters generally being more stable than tocopherol itself. U.S. Patent No. 2,248,861 to Schutt, discloses the use of tocopherol acetate, tocopherol succinate, tocopherol propionate, and tocopherol oleate for preventing deleterious effects to skin of solar radiation.

In a preferred embodiment, a final composition according to the present invention comprises from about 0.01% to about 2.0% of tocopherol acetate, from about 0.01% to about 2.0% of retinyl palmitate, and from about 0.01% to about 12.5% of ascorbic acid.

#### 6. Hydroxy Acid Component/Exfoliating Agent

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Alpha hydroxyacids and alpha ketoacids are used in topical treatment of skin disorders associated with disturbed keratinization or inflammation. These skin disorders include dry skin, dandruff, keratoses, acne, psoriasis, eczema, and pruritus, warts, and herpes. Glycolic acid is the smallest molecule of the alpha hydroxy acids allowing for enhanced penetration into the dermal layers when conditions warrant. It is commercially available as a white crystalline compound that is about 99% pure and also as a 70% aqueous solution. Skin response to glycolic acid depends not only on its concentration and pH but also on other factors such as the amount of free acid delivered to the skin, the duration of contact, preparation of the skin and the condition of the skin before treatment. The preferred concentration of hydroxy and keto acids in the present invention is 5% however an acceptable range is from 0.0% up to 70% by weight. Other hydroxy and keto acids may be used in accordance with acceptable pharmaceutical/cosmetic compounding know how.

## 7. Buffers.

The pH value of the carrier using Aloe Vera is about 4.0 before the consumer combines it with the ascorbic acid wherein it then is in the range of 3.4 to 3.7. If the resultant pH is slightly below or at the lower end of the indicated range, all that is required to adjust the pH to a desired higher value within the indicated range is to add an alkaline additive such as is commonly utilized in cosmetic formulations for such purpose. Although triethanolamine is preferred, other suitable alkalizing agents include potassium carbonate, sodium hydroxide, potassium hydroxide, sodium bicarbonate and the like. If deemed necessary to change or adjust the pH to a lower value, any suitable cosmetically acceptable acidifying agent known in the art may be used.

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Preferably the composition as combined by the consumer is applied to the skin via chronic topical application of a safe and effective amount of the composition to regulate wrinkles of human skin. The amount of actives and frequency of topical application to the skin can vary widely, depending upon personal needs, level of wrinkling present, rate of further wrinkle formation and/or atrophy, and the level of regulation desired but it is suggested as an example that topical application range from about once weekly to about three times daily, preferably about one to two times per day. The composition for topical application will comprise from about 0.01% to about 50%, preferably from about 0.1% to about 20%, more preferably from about 5% to about 15% of the ascorbic acid. By "chronic" application, it is meant herein that the period of topical application may be over the lifetime of the subject, preferably for a period of at least about three weeks, more preferably from about six months to indefinitely, thereby resulting in continuous regulation of wrinkles in human skin.

The compositions and methods of the present invention involve combining at or near the time of first use a safe and effective amount of the ascorbic acid or its derivatives with a safe and effective amount of a pharmaceutically acceptable carrier having minimum aqueous content, having preferably an hydroxy or keto acid and one or more antioxidant radical scavenging agents, simultaneously applied to the skin.

A safe and effective amount of carrier is from about 50% to about 99.9%, preferably from about 75% to about 80%, of the composition. Any substantially anhydrous pharmaceutically acceptable carrier may be used, however, the preferred carrier is stabilized aloe vera gel.

#### 8. Plant Extracts

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The use of calendula, chamomile, arnica and green tea extracts is optional, however, if used, each preferably comprises 0.1% of the vehicle composition. Calendula extract provides firming and anti-edema properties. Chamomile extract provides soothing properties. Arnica extract is thought to possess anti-inflammatory and analgesic effects. Green tea extract is an antioxidant with soothing qualities. Other substantially anhydrous plant extracts commonly known within the cosmetic art may be used.

#### 9. Preservatives

The composition can further comprise a preservative component to retard microbial and mold growth in the composition, which is typically manufactured under clean but non-sterile conditions. One or more preservatives can also act as stabilizers. The preferred preservative component being selected from the group consisting of disodium EDTA, trisodium EDTA, and tetrasodium EDTA, methylparaben, propylparaben, butylparaben and diazolidinyl urea or other commonly known preservatives within the cosmetic art. One preferred composition according to the present invention includes from about 0.01% to about 1.0% of tetrasodium EDTA from about 0.01% to about 1.0% of methylparaben, and 0.01 to about 1.0% diazolidinyl urea.

#### 10. Fragrance

Preferably the composition according to the present invention

comprises fragrance, the use of which is well known in the art. The fragrance comprises 0.05% of the vehicle composition, although this can vary depending upon the fragrance used.



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The preferred concentrations of cosmetic components including those which are optional yet preferred are disclosed in Table 3.

5 II. PREPARATION OF COSMETIC COMPOSITIONS

The various mixtures and the sequences in which they are prepared and combined for the preparation of the cosmetic compositions according to the present invention are described below. The sequences can be combined in a number of orders,  
10 of which the following disclosed below is representative but not exclusive. The object of the mixing sequence as referred to ingredients in Table 3 is to prepare a smooth and homogenous composition.

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## PHARMACEUTICALLY ACCEPTED CARRIER

- Step 1 Heat phase A in main vessel to 70 degrees Centigrade. Remove from heat.
- Step 2 Premix phase B and heat until melted.
- 5 Step 3 Add phase B to main batch.
- Step 4 Cool batch to 45 degrees Centigrade.
- Step 5 Add premixed phase C to batch.
- Step 6 Add phase D.
- Step 7 Premix phase E and add to batch.
- 10 Step 8 Premix phase F and add to batch
- Step 9 Cool to room temperature and submit to QC (Quality Control) lab

## VITAMIN C COMPONENT

- 15 Step 10 In a separate vessel premix phase G
- Step 11 Submit sample to QC lab

## ADVANTAGES OF THE INVENTION

- Cosmetic compositions and the methods according to the present invention provide photoprotection, protection from damage by free radicals, and regulation of wrinkling and other skin disorders associated with chronologic, extrinsic and intrinsic aging processes while, providing a compositions and methods of topically applying vitamin C in a fresh, stable, and active form combined with a moisturizing carrier by the consumer at or near to time of first application to the skin. This virtual point of use combination and limited quantity of batch created per combination by the consumer protects against degradation and instability as is common of those compositions combined by the manufacturer containing vitamin C and those of larger quantity available for extended period of use times beyond the stability range of vitamin C. The ingredients in the final composition after being combined

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by consumer are believed to act synergistically with minimal degradation of vitamin C during expected period of total consumption by user. The present invention as packaged in a kit is designed to be for repeated use, and totally consumed  
5 in substantially stable condition over preferably a two week period. Each combined composition acts to regulate wrinkling associated with aging.

Although the present invention has been described in considerable detail with respect to certain preferred  
10 versions thereof, other versions are possible. Therefore, the spirit and scope of the appended claims should not be limited to the descriptions of the preferred versions contained herein.

Based on the information given in this detailed  
15 description of the invention, it is readily apparent that the invention provides an excellent skin rejuvenating and wrinkle regulating method and modality consisting primarily of an array of predominantly physiologic components, which when combined at or near the time of use have a profound  
20 synergistic beneficial effect upon application to aged and photo-damaged skin. In essence, the present invention treats dry, wrinkled, and aged skin as well as accelerates, augments, and enhances the skin's inherent repair and maintenance mechanisms through application of stable vitamin  
25 C combined with a pharmaceutically acceptable carrier by the consumer at or near time of first use.

Since special individual skin conditions may warrant changes and modifications of the present invention and can be made readily by those skilled in the art without departing  
30 from the basic concept of the present invention, the present invention shall not be limited except by the scope of the appended claims.

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Cosmetic compositions according to the present invention can further comprise other components used in the cosmetic art, such as pigments and other conventional excipients. The use of such ingredients is well known in the art and need not be described here.

All of the compositions and/or methods disclosed and claimed herein can be made and executed without undue experimentation in light of the present disclosure. While the compositions and methods of this invention have been described in terms of preferred embodiments, it will be apparent to those of skill in the art that variations may be applied to the compositions and/or methods and in the steps or in the sequence of steps of the method described herein without departing from the concept, spirit and scope of the invention. More specifically, it will be apparent that certain agents which are both chemically and physiologically related may be substituted for the agents described herein while the same or similar results would be achieved. All such similar substitutes and modifications apparent to those skilled in the art are deemed to be within the spirit, scope and concept of the invention as defined by the claims.

All patents referenced herein are specifically incorporated.

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## CLAIMS

I Claim:

1. A method of regulating wrinkles and the damaging effects  
5 of aging on human skin comprising the steps of the consumer  
combining ascorbic acid or its derivatives with a  
pharmaceutically acceptable carrier at or near the time of  
first use; applying said final combined composition to the  
skin to be treated; repeating the application of the final  
10 composition periodically until the entire quantity of said  
final combined composition is totally consumed.

2. The method of claim 1, wherein the carrier is stabilized  
aloe vera gel.

15

3. The method of claim 2, wherein the carrier further  
comprises glycolic acid.

4. The method of claim 3, wherein the carrier further  
20 comprises vitamin A or its derivatives.

5. The method of claim 4 wherein the carrier further  
comprises vitamin E or its derivatives.

25 6. The method of claim 1, wherein the carrier is in a form  
selected from the group consisting of lotions, creams,  
solutions, sera, and gels.

7. The method of claim 1, wherein the carrier further  
30 comprises molecules selected from the group consisting of  
hydroxyacids, retinoids, and tocopherol, and mixtures  
thereof.

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8. The method of claim 7, wherein the carrier further comprises molecules selected from the group consisting of moisturizers, emulsifiers, anti-inflammatory agents, soothing agents, vitamins, buffers, chelating agents, plant extracts, 5 fragrance, and preservatives.

9. A wrinkle regulating and moisturizing dermatological composition consisting essentially of the formulation in percent by weight:

|    |       |                               |      |
|----|-------|-------------------------------|------|
| 10 |       | stabilized aloe vera gel      |      |
|    |       | 72.00                         |      |
|    |       | ascorbic acid (vitamin C)     |      |
|    | 10.00 |                               |      |
| 15 |       | glycolic acid                 |      |
|    |       | 5.00                          |      |
|    |       | isocetheth-20                 |      |
|    |       | 2.50                          |      |
|    |       | hyaluronic acid               |      |
| 20 |       | 0.50                          |      |
|    |       | chamomile extract             |      |
|    |       | 0.10                          |      |
|    |       | calendula extract             |      |
|    |       | 0.10                          |      |
| 25 |       | green tea extract             |      |
|    |       | 0.10                          |      |
|    |       | arnica extract                |      |
|    |       | 0.10                          |      |
|    |       | alpha tocopherol (vitamin E)  |      |
| 30 |       | 0.50                          |      |
|    |       | retinyl palmitate (vitamin A) |      |
|    |       | 0.10                          |      |
|    |       | methylparaben                 |      |
|    |       | 0.20                          |      |
| 35 |       | diazolidinyl urea             |      |
|    |       | 0.30                          |      |
|    |       | tetrasodium EDTA              |      |
|    |       | 0.10                          |      |
|    |       | sodium metabisulfite          |      |
| 40 |       | 0.25                          |      |
|    |       | triethanolamine               |      |
|    |       | 5.00                          |      |
|    |       | MSM                           |      |
|    |       | 0.10                          |      |
| 45 |       | Fragrance                     |      |
|    |       |                               | 0.05 |

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deionized water

3.00

10. A topical dermatological composition for regulating wrinkles and the other adverse effects of aging on the skin, said composition consisting essentially of, separately packaged ascorbic acid or its derivatives and a substantially anhydrous pharmaceutically acceptable carrier combined together by the user at or near the time of first use.

10

11. A topical dermatological composition for regulating wrinkles and other aging related conditions of the skin, said composition consisting essentially of, ascorbic acid or its derivatives, as a separately packaged active ingredient combined with stabilized aloe vera gel by the consumer at or near the time of first use, the combined composition being applied periodically to the human skin in an amount sufficient to provide an effective quantity of ascorbic acid to the skin to be treated and providing a combined composition which is substantially stable over the expected period of use by the consumer.

12. A method of regulating wrinkles and other damaging effects of the aging process on skin comprising the steps of separately packaging, then combining the ascorbic acid or its derivatives and MSM, with the other ingredients listed in the composition of claim 9 then topically applying the combined composition periodically to the skin to be treated, then repeating the process once the combined composition has been totally consumed.

13. A kit for regulating wrinkles and the damaging effects of aging on the human skin comprising:

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(a) a first composition comprising a safe and effective amount of ascorbic acid (vitamin C) or its derivatives; and  
(b) a second composition comprising approximately a two week supply of substantially anhydrous pharmaceutically acceptable carrier selected from the group consisting of lotions, creams, solutions, sera, and gels wherein said carrier further comprises a safe and effective amount of an active ingredient selected from the group consisting of one or more of (i) an exfoliating agent; (ii) an emulsifier; (iii) soothing agent; (iv) an anti-oxidant; (v) a humectant/moisturizer; (vi) an anti-inflammatory; (vii) a skin protectant; (viii) a plant extract; and (ix) a solvent; derivatives thereof; and mixtures thereof, wherein the first and second compositions are combined at or near the time of use by the consumer and periodically applied to the skin until said combined compositions are total consumed.

14. A kit according to claim 13 wherein the first composition comprises from about .01% to about 15% of ascorbic acid (vitamin C) or its derivatives.

15. A kit according to claim 13 wherein the first composition further comprises methylsulfonylmethane.

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16. A kit for regulating wrinkles and the adverse effects of aging on human skin comprising:

(a) a safe and effective amount of a first composition comprising ascorbic acid C or its derivatives;

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(b) a second composition comprising stabilized Aloe Vera gel as a pharmaceutically acceptable carrier;



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wherein said first and second compositions are physically combined by the consumer at or near the time of first use, said consumer applying a thin layer of said combination of  
5 said first and second compositions to the skin in need of treatment, said consumer reapplying said combination of compositions to the same skin situs at periodically regular intervals until said combination of said first and second compositions is totally consumed.

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17. A kit according to claim 15 wherein said pharmaceutically acceptable carrier is stabilized aloe vera gel.

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18. A wrinkle reducing and moisturizing topical dermatological composition comprising:

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stabilized aloe vera gel  
ascorbic acid (vitamin C)  
glycolic acid  
hyaluronic acid  
alpha tocopherol (vitamin E)  
retinyl palmitate (vitamin A)

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19. A wrinkle reducing and moisturizing topical dermatological composition comprising:

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a substantially anhydrous pharmaceutically acceptable carrier selected from the group consisting of lotions, creams solutions, sera, and gels;

ascorbic acid (vitamin C) or its derivatives;  
an hydroxy acid;  
tocopherol (vitamin E) or its derivatives; and  
a retinoid (vitamin A) or its derivatives

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wherein said ascorbic acid or its derivatives is only added to the remaining ingredients by the consumer at or near the time of first use.

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20. A method of regulating wrinkles and the adverse skin conditions associated with aging on human skin by topically and periodically applying the composition of claim 19 to human skin.

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**AMENDED CLAIMS**

[received by the International Bureau on 02 January 2002 (02.01.02)]

**Amended claim 12 has been amended and claim 21 has been added. Claims 1-11 and 13-20 remain unchanged**

**I Claim:**

1. A method of regulating wrinkles and the damaging effects of aging on human skin comprising the steps of the consumer combining ascorbic acid or its derivatives with a pharmaceutically acceptable carrier at or near the time of first use; applying said final combined composition to the skin to be treated; repeating the application of the final composition periodically until the entire quantity of said final combined composition is totally consumed.

2. The method of claim 1, wherein the carrier is stabilized aloe vera gel.

3. The method of claim 2, wherein the carrier further comprises glycolic acid.

4. The method of claim 3, wherein the carrier further comprises vitamin A or its derivatives.

5. The method of claim 4 wherein the carrier further comprises vitamin E or its derivatives.

6. The method of claim 1, wherein the carrier is in a form selected from the group consisting of lotions, creams, solutions, sera, and gels.

7. The method of claim 1, wherein the carrier further comprises molecules selected from the group consisting of hydroxyacids, retinoids, and tocopherol, and mixtures thereof.

8. The method of claim 7, wherein the carrier further comprises molecules selected from the group consisting of moisturizers, emulsifiers, anti-

inflammatory agents, soothing agents, vitamins, buffers, chelating agents, plant extracts, fragrance, and preservatives.

9. A wrinkle regulating and moisturizing dermatological composition consisting essentially of the formulation in percent by weight:

|       |                               |      |
|-------|-------------------------------|------|
|       | stabilized aloe vera gel      |      |
|       | 72.00                         |      |
|       | ascorbic acid (vitamin C)     |      |
| 10.00 | glycolic acid                 |      |
|       | 5.00                          |      |
|       | isocetheth-20                 |      |
|       | 2.50                          |      |
|       | hyaluronic acid               |      |
|       | 0.50                          |      |
|       | chamomile extract             |      |
|       | 0.10                          |      |
|       | calendula extract             |      |
|       | 0.10                          |      |
|       | green tea extract             |      |
|       | 0.10                          |      |
|       | arnica extract                |      |
|       | 0.10                          |      |
|       | alpha tocopherol (vitamin E)  |      |
|       | 0.50                          |      |
|       | retinyl palmitate (vitamin A) |      |
|       | 0.10                          |      |
|       | methylparaben                 |      |
|       | 0.20                          |      |
|       | diazolidinyl urea             |      |
|       | 0.30                          |      |
|       | tetrasodium EDTA              |      |
|       | 0.10                          |      |
|       | sodium metabisulfite          |      |
|       | 0.25                          |      |
|       | triethanolamine               |      |
|       | 5.00                          |      |
|       | MSM                           |      |
|       | 0.10                          |      |
|       | Fragrance                     | 0.05 |
|       | deionized water               |      |
|       | 3.00                          |      |

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10. A topical dermatological composition for regulating wrinkles and the other adverse effects of aging on the skin, said composition consisting essentially of, separately packaged ascorbic acid or its derivatives and a substantially anhydrous pharmaceutically acceptable carrier combined together by the user at or near the time of first use.

11. A topical dermatological composition for regulating wrinkles and other aging related conditions of the skin, said composition consisting essentially of, ascorbic acid or its derivatives, as a separately packaged active ingredient combined with stabilized aloe vera gel by the consumer at or near the time of first use, the combined composition being applied periodically to the human skin in an amount sufficient to provide an effective quantity of ascorbic acid to the skin to be treated and providing a combined composition which is substantially stable over the expected period of use by the consumer.

12. A method of maintaining stability of ascorbic acid prior to application by a user and regulating wrinkles and other damaging effects of the aging process on skin comprising the steps of (a) separately providing ascorbic acid or its derivatives and MSM from the other ingredients listed in the composition of claim 9, (b) combining all ingredients at or near the time of application, and (c) topically applying the combined composition periodically to the skin to be treated.

13. A kit for regulating wrinkles and the damaging effects of aging on the human skin comprising:

(a) a first composition comprising a safe and effective amount of ascorbic acid (vitamin C) or its derivatives; and

(b) a second composition comprising approximately a two week supply of substantially anhydrous pharmaceutically acceptable carrier selected from the group consisting of lotions, creams, solutions, sera, and gels wherein said carrier further comprises a safe and effective amount of an active ingredient selected from the group consisting of one or more of (i) an exfoliating agent; (ii) an emulsifier; (iii) soothing agent; (iv) an anti-oxidant; (v) a humectant/moisturizer; (vi) an anti-inflammatory; (vii) a skin protectant; (viii) a plant extract; and (ix) a solvent; derivatives thereof; and mixtures thereof,

wherein the first and second compositions are combined at or near the time of use by the consumer and periodically applied to the skin until said combined compositions are total consumed.

14. A kit according to claim 13 wherein the first composition comprises from about .01% to about 15% of ascorbic acid (vitamin C) or its derivatives.

15. A kit according to claim 13 wherein the first composition further comprises methylsulfonylmethane.

16. A kit for regulating wrinkles and the adverse effects of aging on human skin comprising:

(a) a safe and effective amount of a first composition comprising ascorbic acid C or its derivatives;

(b) a second composition comprising stabilized Aloe Vera gel as a pharmaceutically acceptable carrier;

wherein said first and second compositions are physically combined by the consumer at or near the time of first use, said consumer applying a thin layer of said combination of said first and second compositions to the skin in need of treatment, said consumer reapplying said combination of compositions to the same skin situs at periodically regular intervals until said combination of said first and second compositions is totally consumed.

17. A kit according to claim 15 wherein said pharmaceutically acceptable carrier is stabilized aloe vera gel.

18. A wrinkle reducing and moisturizing topical dermatological composition comprising:

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stabilized aloe vera gel  
ascorbic acid (vitamin C)  
glycolic acid  
hyaluronic acid  
alpha tocopherol (vitamin E)  
retinyl palmitate (vitamin A)

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19. A wrinkle reducing and moisturizing topical dermatological composition comprising:

a substantially anhydrous pharmaceutically acceptable

carrier selected from the group consisting of lotions, creams solutions, sera, and gels;

ascorbic acid (vitamin C) or its derivatives;  
an hydroxy acid;  
tocopherol (vitamin E) or its derivatives; and  
a retinoid (vitamin A) or its derivatives

wherein said ascorbic acid or its derivatives is only added to the remaining ingredients by the consumer at or near the time of first use.

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20. A method of regulating wrinkles and the adverse skin conditions associated with aging on human skin by topically and periodically applying the composition of claim 19 to human skin.

21. A method of maintaining stability of ascorbic acid prior to application by a user and regulating wrinkles and other damaging effects of the aging process on skin comprising the steps of (a) separately providing ascorbic acid or its derivatives from a delivery vehicle, (b) combining the ascorbic acid or its derivatives with the delivery vehicle at or near the time of application, and (c) topically applying the combined composition.



**STATEMENT UNDER ARTICLE 19 (1)**

This Amendment is responsive to the International Search Report dated November 2, 2001. In that Action, the Authorized Officer cited the combination of Hernandez and Hargraves against claims 1-20. Applicant respectfully traverses the citation and offers the foregoing amendments and following remarks in support thereof.

Claim 12 has been amended and Claim 21 has been added. No new matter has been inserted. Claims 1-21 remain pending in the application. Applicant respectfully requests reconsideration of the Authorized Officer's citations.

As to the citation, Hernandez fails to teach of ingredients such as hydroxy acids or aloe vera forms, and also fails to teach of combining the ingredients at or near the time of use. Hernandez is an example industry attempts to solve the problem of stabilization of ascorbic acid over any significant period (i.e. potency loss and discoloration) from use of liquid based delivery vehicles, such as water. Hernandez provides a composition (ascorbic acid and delivery system) which can remain combined for an extended period of time, prior to use by a consumer, without potency loss or discoloration. To achieve these characteristics an anhydrous delivery vehicle, with no water added, is provided and disclosed by Hernandez. Thus, Hernandez attempts to solve the ascorbic acid stabilization problem by changing the material of the delivery vehicle. However, the elements of composition are

premixed (combined) at the time of manufacture. Hernandez provides absolutely no teaching, disclosure or suggestion of changing the way ascorbic based compositions for lotions and creams are applied by the consumer or the point where the materials of the composition are combined (mixed).

Hargraves discloses a skin care kit, which includes a dispenser for a premixed skin care composition. Though, the disclosure discusses using aloe vera as an element of the composition, Hargraves also fails to provide any teaching, disclosure or suggestion of changing the way ascorbic based compositions for lotions and creams are applied by the consumer or the point where the materials (elements) of the composition are combined (mixed).

Additionally, by combining Hargraves' alleged aloe vera delivery vehicle with Hernandez, it is respectfully submitted, that the Authorized Officer has destroyed the primary teaching of Hernandez of providing an anhydrous delivery vehicle. Aloe vera and glycolic acid are aqueous elements. Furthermore, the Authorized Officer's proposed combination provided in a premixed composition, would result in the stabilization problems discussed above.

Accordingly, in view of the above, applicant respectfully requests a favorable opinion by the Authorized Officer.

If there are any additional charges, including extension of time, please bill our United States Deposit Account No. 13-1130.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/26058

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A61K 7/28, 6/00; A01N 43/08, 25/00

US CL : 424/59, 401; 514/474, 937

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/59, 401; 514/474, 937

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EAST

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|-----------|---|-----------------------|
| Y         | US 5843411 (HERNANDEZ ET AL.) 01 DECEMBER 1998, col. 4, lines 12, 15, 22, 25-29, 55-59, col. 6, table 1   | 1-20                  |
| Y         | US 6013270 (HARGRAVES et al.) 11 JANUARY 2000, col. 2, lines 19-42; col. 30, lines 40-44; col. 33, lines 46-51; col. 34, lines 31-36 and 60-61. | 1-20                  |



Further documents are listed in the continuation of Box C.



See patent family annex.

|   |  |
|---|--|
| * Special categories of cited documents   | "T" Later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| "A" document defining the general state of the art which is not considered to be of particular relevance  | "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| "E" earlier document published on or after the international filing date  | "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "G" document member of the same patent family  |
| "O" document referring to an oral disclosure, use, exhibition or other means  |  |
| "P" document published prior to the international filing date but later than the priority date claimed  |  |

Date of the actual completion of the international search

19 SEPTEMBER 2001

Date of mailing of the international search report

02 NOV 2001

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